

DETAILED ACTION

The receipt is acknowledged of applicants' amendment filed 05/02/2011.

Claims 8-11, 13, 14, 16, 20, 22-24, 29, 30, 32-38, and 40-55 previously presented, and claims 56-58 are currently added.

Claims 8-11, 13, 14, 16, 20, 22-24, 29, 30, 32-38, and 40-58 are currently pending and included in the prosecution.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 8-11, 13, 14, 16, 20-23, 29, 30, 32, 40-42, 45-49, 53-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kogan et al. (US 4,910,205) in view of Aslanian et al. (US 6,103,735) both references are of record.

Applicant Claims

Applicant s' claim 8 is directed to a method of effectively treating seasonal allergic rhinitis, chronic idiopathic urticaria, or both conditions in a human patient, comprising administering loratadine transdermally to the human patient by applying a transdermal delivery system comprising (i) an active agent consisting of loratadine or a pharmaceutically acceptable salt thereof, (ii) a polymer, (iii) a softening agent; and (iv) a solvent, to the skin of a patient, and maintaining said transdermal delivery system in contact with the skin of the patient for at least 5 days, said transdermal delivery system maintaining an effective mean relative release rate to provide a therapeutic blood level

of said loratadine within three days from the initiation of the dosing interval, and thereafter maintaining a therapeutic blood level until the end of at least the five-day dosing interval, said transdermal delivery device maintaining a plasma level of loratadine at steady state of about 3 ng/ml;

said transdermal delivery system having a mean relative release rate of from about $2.8 \mu\text{g}/\text{cm}^2/\text{hr}$ to about $16.2 \mu\text{g}/\text{cm}^2/\text{hr}$ of the transdermal delivery system surface area at 24 hours;

from about $2.3 \mu\text{g}/\text{cm}^2/\text{hr}$ to about $13.7 \mu\text{g}/\text{cm}^2/\text{hr}$ of the transdermal delivery system surface area at 48 hours; from about $2.0 \mu\text{g}/\text{cm}^2/\text{hr}$ to about $11.9 \mu\text{g}/\text{cm}^2/\text{hr}$ of the transdermal delivery system surface area at 72 hours;

and a mean relative release rate of from about $1.8 \mu\text{g}/\text{cm}^2/\text{hr}$ to about $9.9 \mu\text{g}/\text{cm}^2/\text{hr}$ of the transdermal delivery system surface area at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water.

Applicants' claim 20 is directed to a transdermal delivery system comprising (i) an active agent consisting of loratadine or a pharmaceutically acceptable salt thereof, (ii) a polymer, (iii) a softening agent; and (iv) a solvent,

the transdermal delivery system provides a mean relative release rate of from about $2.8 \mu\text{g}/\text{cm}^2/\text{hr}$ to about $16.2 \mu\text{g}/\text{cm}^2/\text{hr}$ of the transdermal delivery system surface area at 24 hours;

from about $2.3 \mu\text{g}/\text{cm}^2/\text{hr}$ to about $13.7 \mu\text{g}/\text{cm}^2/\text{hr}$ of the transdermal delivery system surface area at 48 hours;

from about $2.0 \mu\text{g}/\text{cm}^2/\text{hr}$ to about $11.9 \mu\text{g}/\text{cm}^2/\text{hr}$ of the transdermal delivery system surface area at 72 hours;

and from about $1.8 \mu\text{g}/\text{cm}^2/\text{hr}$ to about $9.9 \mu\text{g}/\text{cm}^2/\text{hr}$ of the transdermal delivery system surface area at 96 hours; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin and said cell having a receptor chamber containing a 40:60 mixture of ethanol:water; said transdermal delivery system maintaining an effective mean relative release rate to provide a therapeutic blood level of said loratadine within 36 hours from the initiation of the dosing interval, and a plasma level of loratadine of at least about $0.1 \mu\text{g}/\text{ml}$ by about 6 hours after application of said transdermal delivery system onto the skin of a human patient; said transdermal delivery system maintaining a therapeutic blood level until the end of at least a five-day dosing interval and a plasma level of loratadine at steady state of about 3 ng/ml.

Applicants' claim 46 is directed to a method of effectively treating seasonal allergic rhinitis, chronic idiopathic urticaria, or both conditions in a human patient, comprising administering loratadine transdermally to the human patient by applying a transdermal delivery system containing loratadine or a pharmaceutically acceptable salt thereof to the skin of a patient, and maintaining said transdermal delivery system in contact with the skin of the patient for at least 5 days, said transdermal delivery system maintaining an effective mean relative release rate to provide a therapeutic blood level

of said loratadine within three days from the initiation of the dosing interval, and thereafter maintaining a therapeutic blood level until the end of at least the five-day dosing interval, said transdermal delivery device maintaining a plasma level of loratadine at steady state of about 3 ng/ml;

said transdermal delivery device comprising a backing layer which is substantially impermeable to the loratadine or pharmaceutically acceptable salt thereof, and a reservoir layer consisting essentially of 20 to 90% by weight of a polymeric matrix, 0.1 to 30% by weight of a softening agent; 0.1 to 20% by weight of loratadine base or of a pharmaceutically acceptable salt thereof and 0.1 to 30% by weight of a solvent, for the loratadine or salt thereof;

said transdermal delivery system having a mean relative release rate of from about 2.8 $\mu\text{g}/\text{cm}^2/\text{hr}$ to about 16.2 $\mu\text{g}/\text{cm}^2/\text{hr}$ of the transdermal delivery system surface area at 24 hours;

from about 2.3 $\mu\text{g}/\text{cm}^2/\text{hr}$ to about 13.7 $\mu\text{g}/\text{cm}^2/\text{hr}$ of the transdermal delivery system surface area at 48 hours;

from about 2.0 $\mu\text{g}/\text{cm}^2/\text{hr}$ to about 11.9 $\mu\text{g}/\text{cm}^2/\text{hr}$ of the transdermal delivery system surface area at 72 hours;

and a mean relative release rate of from about 1.8 $\mu\text{g}/\text{cm}^2/\text{hr}$ to about 9.9 $\mu\text{g}/\text{cm}^2/\text{hr}$ of the transdermal delivery system surface area at 96 hours ; as determined via an in-vitro permeation test utilizing a Valia-Chien cell where the membrane is a human cadaver skin, said cell having a receptor chamber containing a 40:60 mixture of ethanol:water.

The recited plasma levels and release rates are broadened by the term “about”

Determination of the Scope and Content of the Prior Art
(MPEP §2141.01)

Kogan teaches a transdermal delivery system of loratadine for the treatment of allergic conditions (abstract). The system is formed of patch applied to skin for a specific period of time to permit the penetration of a desired amount of loratadine through the skin. The patch comprises a reservoir having 10-20% loratadine; 50-60% solvent; polymer (cellulose polymer), and 20-35% fatty acid esters, i.e. softening agents (col.2, lines 19-29). The patch further comprises a backing layer and a release liner (col.2, line 64; col.3, line 6). The patch will be worn from one to four days and provides a total daily dose of 0.5 to 5 mg (col.2, lines 28-34), which is from 500 μg to 5000 μg per day for one to four days. The reference disclosed patch size of 15 cm^2 , i.e. average daily released dose of 500 $\mu\text{g}/15 \text{ cm}^2/\text{day}$ to 5000 $\mu\text{g}/15 \text{ cm}^2/\text{day}$. When the dose provided by 15 cm^2 patch is divided by 15 will provide the dose per cm^2 , that is calculated 33.3 $\mu\text{g}/\text{cm}^2/\text{day}$ to 333 $\mu\text{g}/\text{cm}^2/\text{day}$, which when divided by 24 will provide the hourly dose which is calculated to be 1.4 $\mu\text{g}/\text{cm}^2/\text{hr}$ to 14 $\mu\text{g}/\text{cm}^2/\text{hr}$. The value from 1.4 $\mu\text{g}/\text{cm}^2/\text{hr}$ to 14 $\mu\text{g}/\text{cm}^2/\text{hr}$ represents the mean average release rate disclosed by the reference, and applicant claim mean average release rate from 1.8 $\mu\text{g}/\text{cm}^2/\text{hr}$ to 9.9 $\mu\text{g}/\text{cm}^2/\text{hr}$, which falls within the values disclosed by the reference. The reference disclosed that the dose may be varied depending on the size and age of the patient, and may also depend upon the severity of the condition being treated (col.3, lines 56-60). The frequency of dosage

application can be once every 3 days to once every 7 days (col.4, lines 5-10). The claimed delivery rates are met by the reference because the claimed rates are broadened by the term “about” and inclusive of the rates disclosed by the prior art. Kogan does not disclose any other active agent in the formulation as required by claims 56-58.

With respect to the claimed release rates that are determined by Valia-Chein cell, the prior art is silent regarding the test method and the art does not appear to rely on, or teach the test method. The Patent Office is not equipped with test facilities for result testing. Hence, the instantly claimed release rates are met by the prior art.

**Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)**

Kogan does not explicitly teach the same plasma level of loratadine as instantly claimed. However, Kogan teaches the same daily and hourly delivery rate of loratadine for the same period of time as instantly claimed, as calculated by the examiner, and this implies that plasma level of loratadine displayed by Kogan would be the same as claimed. Further, the structure *as claimed* is the same as the prior art and providing 7 days of treatment..

In any event, Aslanian teaches pharmaceutical composition for treating allergic rhinitis comprising therapeutically effective amount of H₁ antagonist (abstract; col.6, lines 8-15). The reference teaches that the pharmaceutical composition is deliverable in transdermal patch (col.7, lines 8-11). A single dosage form of the composition

comprises from 1-200 mg of H₁ antagonist and actual dose may be varied depending upon patient's age, sex, weight, and severity of the condition being treated (col.7, lines 23-25; col.2, lines 33-35). Preferred H₁ antagonist is loratadine (col.8, line 66; claims 21 and 32). In present example 8 applicants use 0.12 gm loratadine, i.e. 120 mg.

Therefore, in the light of Aslanian teaching, at the time of the invention it was known to load 120 mg of loratadine in a single dosage form as a therapeutically effective dose of loratadine for treating allergic rhinitis.

Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat allergic rhinitis using transdermal device comprising loratadine, solvent, skin softening agent and polymer as taught by Kogan, and use 1-200 mg of loratadine in the transdermal device as taught by Aslanian. One would have been motivated to do so because Aslanian teaches such an amount in a single dosage form, including transdermal patch, is the therapeutically effective dose of loratadine for treating allergic rhinitis. One would reasonably expect effectively treating allergic rhinitis using transdermal device comprising from 1-200 mg loratadine. One would further reasonably expect obtaining plasma levels as instantly claimed because the device taught from the combination of Kogan and Aslanian comprises the same amount of loratadine, solvent, polymer and skin softener and deliver loratadine in the same rate as instantly claimed. Therefore, since the instant specification teaches the same amount

of loratadine and as evidenced by Aslanian this is a known and routine amount to be used by the prior art and Kogan teaches the same transdermal structure and treatment days, one would expect that the properties to flow from the combined teaching.

Regarding the claimed release rate of loratadine, Kogan teaches the same mean relative release rate as instantly claim, and combination of Kogan and Aslanian teaches the device comprising the same ingredients and amounts as instantly claimed. Therefore, the amounts and corresponding ratio overlaps with the instant claims. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. **See MPEP 2144.05 [R-5].**

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

The determination of the relative release rate via an in-vitro permeation test utilizing a Valia-Chien cell is not part of the claimed method of treating allergic rhinitis; or even a part of the transdermal device that provide particular plasma levels of loratadine. It is only an in-vitro diagnostic test that is expected to provide the same results obtained from two similar delivery devices tested under the same circumstances, and the recitation of this in-vitro test does not impart patentability to claims directed to method of treating allergic rhinitis or claims directed to transdermal device applied to patients to provide specific plasma levels of loratadine, i.e. in vivo use.

5. Claims 35, 36, 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Kogan and Aslanian and further in view of Venkateshwaran (US 5,912,009) of record.

Applicant Claims

Applicant s' claims 35 and 43 recite specific polymers, and claims 36 and 44 recite specific skin softeners.

Determination of the Scope and Content of the Prior Art

(MPEP §2141.01)

The combined teachings of Kogan and Aslanian are previously discussed in this office action.

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

Although Kogan teaches polymer and skin softeners in the transdermal composition, however, does not explicitly teach specific polymers and skin softener as instantly claimed by claims 35, 36, 43 and 44.

Venkateshwaran teaches transdermal device to enhance delivery of drugs and not limited to any specific drug (abstract; col.4, lines 3-5). Drugs include antihistaminics (col.5, line 9). The device comprises matrix composition comprising pressure sensitive adhesive polymer including 50-99.75% of acrylate and rubber adhesive and glycols

(col.4, lines 52-65; col.8, lines 18-42). The composition further comprises fatty acids esters including those of capric and caprylic acid (col.7, lines 7-9). The composition taught by the reference enhances transdermal delivery of drugs and has good skin tolerability with minimal risks of skin toxicity and irritation (col.3, lines 27-31).

Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat allergic rhinitis using transdermal device comprising composition comprising loratadine, polymer, skin softening agent and solvent as taught by Kogan combined with Aslanian, and use acrylic or rubber polymers and further use glycol and/or esters of capric or caprylic acid taught by Venkateshwaran in the composition. One would have been motivated to do so because Venkateshwaran teaches that such a composition enhances transdermal delivery of drugs and has good skin tolerability with minimal risks of skin toxicity and irritation. One would reasonably expect treating allergic rhinitis using transdermal device comprising composition comprising loratadine, acrylic or rubber adhesive, glycol and esters of capric or caprylic acid wherein the composition is not toxic to the skin nor irritating to the user, therefore improves patient's compliance.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the

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instantly claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

6. Claims 24, 33-35, 37, 38 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Kogan and Aslanian and further in view of Anhauser et al. (US 6,315,854) of record.

Applicant Claims

Applicant s' claims 24, 35 and 43 recite specific polymers, claims 37 and 38 recite specific solvent, and claims 33 and 34 recite material of the backing.

Determination of the Scope and Content of the Prior Art

(MPEP §2141.01)

The combined teachings of Kogan and Aslanian are previously discussed in this office action.

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

Although Kogan teaches polymer and solvents in the transdermal composition, however, does not explicitly teach specific polymers and solvents as instantly claimed by claims 24, 35, 37, 38 and 43, or material of the backing as instantly claimed by claims 33-34.

Anhauser teaches transdermal device for continuous delivery of many active agents with minimal loss of active agent while is looking like a regular band-aid (abstract; col.1, lines 7-22; col.4, lines 1-10). The device comprises reservoir containing the active agent, polymer, and additives. The backing is flexible or non-flexible or containing aluminum foil. Polymers include acrylate, rubber or block copolymers. One of the preferred additives is glutaric acid monomethyl ester. (See col.3, lines 8-34; col.5, lines 15-16).

Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat allergic rhinitis using transdermal device comprising composition comprising loratadine, polymer, skin softening agent and solvent as taught by Kogan combined with Aslanian, and use acrylic or rubber polymers and add glutaric acid monomethyl ester, as well as use flexible or non-flexible backing as taught by Anhauser. One would have been motivated to do so because Anhauser teaches that a transdermal comprising such a composition provides continuous delivery of many active agents with minimal loss of active agent while is looking like a regular band-aid. One would reasonably expect treating allergic rhinitis using transdermal device comprising composition comprising loratadine, acrylic or rubber adhesive, and glutaric acid monomethyl ester, wherein the device provides continuous drug delivery while acceptably appealing to the user.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

7. Claims 50-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Kogan with Aslanian and further in view of Venkateshwaran and Anhauser.

Applicant Claims

Applicant s' claims 50-52 recite specific solvents and skin softeners.

Determination of the Scope and Content of the Prior Art

(MPEP §2141.01)

The combined teachings of Kogan, Aslanian are previously discussed in this office action.

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

Although Kogan teaches skin softeners and solvents in the transdermal composition, however, does not explicitly teach specific skin softener and solvent as instantly claimed by claims 50-52.

Specific skin softeners are taught by Venkateshwaran and specific solvents are taught by Anhauser.

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP §2142-2143)

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat allergic rhinitis using transdermal device comprising composition comprising loratadine, polymer, skin softening agent and solvent as taught by Kogan combined with Aslanian, and use glycols taught by Venkateshwaran and glutaric acid monomethyl ester taught by Anhauser in the transdermal composition. One would have been motivated to do so because Venkateshwaran teaches that composition comprising glycols enhances transdermal delivery of drugs and has good skin tolerability with minimal risks of skin toxicity and irritation, and because Anhauser teaches that transdermal composition comprising glutaric acid monomethyl ester provides continuous delivery of many active agents with minimal loss of active agent while is looking like a regular band-aid. One would reasonably expect treating allergic rhinitis using transdermal device comprising composition comprising loratadine, polymer, glycols, and glutaric acid monomethyl ester, wherein the device is not toxic nor irritating to the skin and provides continuous drug delivery while being acceptably appealing to the user.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the

instantly claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made

Response to Arguments

8. Applicant's arguments filed 05/02/2011 have been fully considered but they are not persuasive.

Applicants argue that the combination of the cited references on its face does not teach or suggest all the elements of the present claims. The Examiner repeatedly stated that the Kogan reference "does not teach the specific delivery profile of loratadine " The Examiner now purports that this deficiency is cured by the Aslanian reference. Aslanian reference cannot cure this deficiency of the Kogan reference as articulated by the Examiner, because the Aslanian reference does not teach or suggest the specific delivery profile of loratadine. Aslanian "The compounds of the invention may also be deliverable transdermally. The transdermal compositions may take the form of creams, lotions, aerosols and/or emulsions and can be included in a transdermal patch of the matrix or reservoir type as a re [sic] conventional in the art for this purpose." This disclosure of the Aslanian reference cannot teach or suggest the feature missing from the Kogan reference (i.e., the specific delivery profile of loratadine).

In response to this argument it is argued that Kogan teaches mean average release rate from $1.4 \mu\text{g}/\text{cm}^2/\text{hr}$ to $14 \mu\text{g}/\text{cm}^2/\text{hr}$ and applicants claim mean average release rate from $1.8 \mu\text{g}/\text{cm}^2/\text{hr}$ to $9.9 \mu\text{g}/\text{cm}^2/\text{hr}$, which falls within the values disclosed by the reference. Further Kogan teaches release for many days. Therefore, the claimed release rates and times are met by the reference. Aslanian is relied upon for teaching the dose of loratadine in grams/milligrams that is used to treat allergic rhinitis. Aslanian teaches pharmaceutical composition for treating allergic rhinitis comprising therapeutically effective amount of H_1 antagonist such as loratadine, wherein a single dosage form of the composition comprises from 1-200 mg of H_1 antagonist. In present example 8 applicants use 0.12 gm loratadine, i.e. 120 mg. Therefore, in the light of

Aslanian teaching, at the time of the invention it was known to load 120 mg of loratadine in a single dosage form as a therapeutically effective dose of loratadine for treating allergic rhinitis. Kogan teaches transdermal delivery and Aslanian suggested transdermal delivery. The same dose of loratadine when delivered transdermally from the same formulation it will inevitably provide the same release rate and steady state release because materials and their properties are inseparable.

Regarding the disclosure of Aslanian of transdermal delivery, the reference teaches and suggested transdermal drug delivery. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

Regarding the claimed release rate of loratadine, Kogan teaches the same mean relative release rate as instantly claimed, and combination of Kogan and Aslanian teaches transdermal device comprising the same ingredients and amounts as instantly

claimed. Hence, the release rate of loratadine from the device taught by the combination of Kogan comprising 1-200 mg as taught by Aslanian will inevitably provide the same release rate and steady state. Therefore, the amounts and corresponding ratio overlaps with the instant claims. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists.

See MPEP 2144.05 [R-5].

Applicants argue that the rejection imports elements from the specification and it is based on the present specification and impermissibly imports elements from the present specification into the present claims. The Manual of the Patent Examining Procedure states: "Though understanding the claim language may be aided by explanations contained in the written description, it is important not to import into a claim limitations that are not part of the claim. For example, a particular embodiment appearing in the written description may not be read into a claim when the claim language is broader than the embodiment." The Examiner supports the instant rejection by stating on page 10 of the Office Action that that "since the instant specification teaches the same amount of loratadine [as disclosed in the Aslanian reference] ..." it is expected that the claimed properties will flow from the combined teachings of the references. Applicants argue that the present specification, including Example 8, is not "prior art" and therefore cannot be used to support the present rejection. Applicants further submit that the present claims do not recite any loratadine amounts, and therefore, the Examiner's reliance on the 120 mg of loratadine disclosed in Example 8 impermissibly imports limitations from the present specification into the present claims.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA

1971). In the instant case the examiner does not rely on the specification as a prior art, rather relies on Aslanian for teaching the amount of drug and to show it was known in the art at the time of the invention to use such amount in transdermal device to treat rhinitis. Further, as applicants admit, the present claims does not recite amount of the loratadine rather recite what loratadine does in terms of steady state and release rates, therefore, the examiner needs to read the specification to see what amounts of loratadine provides the claimed release profiles. As applicants admit, MPEP states that “Though **understanding the claim language may be aided by explanations contained in the written description**, it is important not to import into a claim limitations that are not part of the claim”. What happened in this case is: the examiner referred to the specification to understand the claims, and not to rely on the specification as prior art, and not to bring limitations from the specification to the claims. The examiner relied on specification to understand what dose provides the claims release rate in order to conduct thorough search. The examiner looked in the specification to find what formulation and amount of drug provide the claimed function. **MPEP § 904 stated that in determining the scope and content of the prior art, Office personnel must first obtain a thorough understanding of the invention disclosed and claimed in the application under examination by reading the specification, including the claims, to understand what the applicant has invented.** The scope of the claimed invention must be clearly determined by giving the claims the “broadest reasonable interpretation consistent with the specification.” See Phillips v. AWH Corp., 415 F.3d 1303, 1316, 75 USPQ2d 1321, 1329 (Fed. Cir. 2005) and MPEP § 2111.

Once the scope of the claimed invention is determined, Office personnel must then determine what to search for and where to search. Therefore, referring to the specification to understand the invention for search purpose is permitted and acceptable by the patent office.

Applicants argue that independent claims 8, 20 and 46 recite that the transdermal delivery system maintains "a steady state plasma concentration of loratadine of about 3 ng/ml" and specific delivery profiles of loratadine that are not taught or suggested by the combination of the cited references. Applicants argue that the steady state plasma concentration of loratadine purportedly suggested by the Kogan reference is different from the steady state concentration of loratadine recited in instant independent claims 8, 20 and 46. The steady state plasma concentration of loratadine purportedly suggested by the Kogan reference can be calculated by using the information provided in the present specification. The present specification describes two formulas for calculating the dosing rate of loratadine. First, the specification states that the dosing rate is "a product of the steady state concentration of loratadine and a representative clearance rate." The steady- steady concentration of loratadine may therefore be calculated by dividing the dosing rate of loratadine by its clearance rate. The clearance rate of loratadine is 196000 ml/hr. The calculated steady state loratadine concentration after administration of the Final Gel of Kogan at approximately steady state is therefore 0.48 ng/ml. This calculated steady state concentration does not overlap with the steady state concentration of "about 3 ng/ml" recited in instant claim 8. The dosing rate at approximate steady state after administration of the Final Gel of the Kogan reference is 2.26 mg/15cm²/day, or 94167 ng/hour. The calculated steady state loratadine concentration after administration of the Final Gel at approximately steady state of the Kogan reference is therefore 0.69 ng/ml. This calculated steady state concentration of loratadine is in sharp contrast to the steady state concentration of "about 3 ng/ml" recited in independent claims 8, 20 and 46.

In response to this argument it is argued that Kogan teaches a transdermal delivery system of loratadine comprising a reservoir having 10-20% loratadine; 50-60% solvent; polymer (cellulose polymer), and 20-35% fatty acid esters, i.e. softening agents. This teachings read on the claimed formulation in its broadest interpretation. The patch will be worn from one to four days and provides a total daily dose of 0.5 to 5 mg (col.2, lines 28-34), which is from 500 µg to 5000 µg per day for one to four days. The

reference teaches formulation comprising the same ingredients as instantly claimed and teaches the same release rate as instantly claimed and the plasma steady state will be inevitable particularly if the same amount of loratadine taught by Aslanian is used in the formulation taught by Kogan. When the dose provided by 15 cm² patch is divided by 15 will provide the dose per cm², that is calculated 33.3 μg/ cm²/day to 333 μg/ cm²/day, which when divided by 24 will provide the hourly dose which is calculated to be 1.4 μg/cm²/hr to 14 μg/cm²/hr. The value from 1.4 μg/cm²/hr to 14 μg/cm²/hr represents the mean average release rate disclosed by the reference, and applicant claim mean average release rate from 1.8 μg/ cm²/hr to 9.9 μg/ cm²/hr, which falls within the values disclosed by the reference. Aslanian teaches the same amount of loratadine in gram/milligram that can be given to treat allergic rhinitis. The claimed steady state is the result of the ingredients used in the formulation and their amounts, and the prior art teaches the claimed ingredients as broadly claimed by claims 8, 20 and 46. According to applicants' calculation, the steady state is the result of the dose and clearance of loratadine, and since clearance is property of loratadine, and the dose of the drug is taught by Aslanian, then the steady state as claimed is expected from the combination of the prior art. *In Alza Corp. v. Mylan Laboratories, Inc.*, 464 F.3d 1286, 80 USPQ2d 1001 (Fed. Cir. 2006), the court found that because the absorption properties of oxybutynin would have been reasonably predictable at the time of the invention, there would have been a reasonable expectation of successful development of a sustained-release formulation of oxybutynin as claimed. The prior art, as evidenced by the specification, had recognized the obstacles to be overcome in development of

sustained-release formulations of highly water-soluble drugs, and had suggested a finite number of ways to overcome these obstacles. The claims were obvious because it would have been obvious to try the known methods for formulating sustained-release compositions, with a reasonable expectation of success. The court was not swayed by arguments of a lack of absolute predictability. The examiner believes the present claims are reasonably expected from the cited prior art.

Applicants argue that a prima facie case of obviousness cannot be established by using the combination of the cited references because the combination of the cited references does not teach or suggest the plasma level of loratadine at steady state recited in the present claims.

In response to this argument, it is argued that, as discussed above the combination of the references will suggested the same release rate of loratadine from transdermal formulation comprising the same ingredient and amount of the drug, and if the same amount of the drug is used, as well as the same formulation, including the polymer used, the permeation enhancer, solvent, etc., then it is inevitably the same claimed steady state is achieved. See previous section of this office action.

Applicants argue that of the cited references does not teach or suggest the limitations of claims 9-11, 13, and 29, 53-55, or new claims 56-58. Applicants thus submit that a prima facie case of obviousness of claim 9 has not been established.

In response to the argument regarding claims 9-11, 13, 29, it is argued the claims are directed to release and effect of loratadine that are inevitably obtained from the device taught by the combination of Kogan and Aslanian. It has been further held that

the discovery of a new action underlying a known process does not make it patentable. *MEHL/Biophile*, 192 F.3d at 1365, 52 U.S.P.Q.2d at 1303. Also, it is irrelevant that the prior art observers did not recognize the property or function of the disputed claim; if the prior art inherently possessed that characteristic, it anticipates. See *Verdeegal Brothers, Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 633, 2 U.S.P.Q.2d 1051, 1054 (Fed. Cir. 1987). This is believed to be applicable here because anticipation is the epitome of obviousness.

Regarding claim 53-55, the claims recite the transdermal device comprises solution of the active agent, and Kogan teaches solvent in the its formulation which will form a solution.

With regard to the new claims 56-58, Kogan does not teach other active agent to treat rhinitis other than loratadine.

Applicants argue that Aslanian reference "discloses compositions which comprise combinations of antagonists of neurokinin receptors and antagonists of histamine receptors, and methods for treating [e.g., allergic rhinitis, and other respiratory diseases] ... with such compositions." The removal of the neurokinin receptor antagonist would destroy the inventive composition of the Aslanian reference.

In response to this argument, it is argued that Aslanian is relied upon for the solely teaching of the anti-allergic effective dose of loratadine. Kogan realized the anti-allergic effect of loratadine by itself without other active agents. The open ended language of the claims "method for....comprising administering loratadine transdermally..." permits the presence of other ingredients, active or inactive, even in major amounts.

Applicants request that the Examiner provides the reasons why the previous rejection argued by the Applicants in the Appeal Brief filed on November 17, 2010 was withdrawn, by referring specifically to the pages and lines of the Appeal Brief which formed the basis for withdrawing the rejection, as required by the MPEP.

In response to this request, at the stage when applicants file an appeal brief, a conference comprising panel of two SPE and the examiner reviewed the rejection and decided that addition to Kogan a reference teaching the same amount of loratadine as used by applicants in their disclosure would make the present claims *prima facie* obvious because the release rate and plasma steady state will inevitably obtained from the combination of such references. Hence Aslanian reference was introduced.

Applicants traverse the rejection over Kogan and Aslanian in view of the Venkateshwaran; the rejection over Kogan and the Aslanian in view of the Anhauser; and the rejection over Kogan and the Aslanian in view of the Venkateshwaran and the Anhauser by arguing that no mention of loratadine in Venkateshwaran and Anhauser.

In response to this argument, it is argued that by Venkateshwaran is relied upon for the solely teaching of the use acrylic or rubber polymers and the use of glycol and/or esters of capric or caprylic acid in transdermal composition for the benefit of enhancing transdermal delivery of drugs while having good skin tolerability with minimal risks of skin toxicity and irritation. Anhauser is relied upon for the solely teaching of the use acrylic or rubber polymers and the use of glutaric acid monomethyl ester in transdermal formulation, as well as the use flexible or non-flexible backing in transdermal devices. Anhauser teaches the benefit that a transdermal device comprising such a composition and backing provides continuous delivery of many active agents with minimal loss of

active agent while is looking like a regular band-aid. Transdermal loratadine is taught by Kogan and Aslanian, and Venkateshwaran and Anhauser are relied upon for teaching limitations of dependent claims.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571)272-0595. The examiner can normally be reached on Monday-Thursday, 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone

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number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

IG

/Isis A Ghali/
Primary Examiner, Art Unit 1611